

In Memoriam

California Medical Association

AYCINENA, JUAN, San Mateo. Died Jul 6, 1991, aged 81. Graduate of University of San Carlos, Guatemala, 1940. Licensed in California in 1943. Dr Aycinena was a member of the San Mateo County Medical Society.



BARNETT, CLAIR B., Corona del Mar. Died Sep 1, 1991, aged 75. Graduate of University of Southern California, Los Angeles, 1944. Dr Barnett was a member of the Orange County Medical Association.



BARTLETT, JOHN C., Orinda. Died Jun 13, 1991, aged 84. Graduate of University of Southern California, Los Angeles, 1937. Licensed in California in 1937. Dr Bartlett was a member of the Alameda-Contra Costa Medical Association.



BATTEN, DOUGLAS H., San Diego. Died Aug 14, 1991, aged 81. Graduate of University of Rochester, Rochester, New York, 1936. Dr Batten was a member of the San Diego County Medical Society.



BERTERO, JULES, Santa Maria. Died Apr 19, 1991, aged 89. Graduate of St Louis University, Missouri, 1929. Licensed in California in 1930. Dr Bertero was a member of the Santa Barbara County Medical Society.



BESCOBY, FELIX J., Upland. Died Jul 11, 1991, aged 68. Graduate of Northwestern University Medical School, Chicago, 1949. Licensed in California in 1949. Dr Bescoby was a member of the San Bernardino County Medical Society.



BOOMER, JOSEPH M., Richmond. Died May 12, 1991, aged 81. Graduate of University of Nebraska, Omaha, 1934. Dr Boomer was a member of the Alameda-Contra Costa Medical Association.

CALVY, WILLIAM J., Anaheim. Died Sep 1991, aged 77. Graduate of University of Wisconsin, Madison, 1939. Dr Calvy was a member of the Orange County Medical Association.



CHANDLER, ARTHUR L., Los Angeles. Died Apr 23, 1991, aged 79. Graduate of Rush Medical College, Chicago, Illinois, 1939. Licensed in California in 1947. Dr Chandler was a member of the Los Angeles County Medical Association.



DOWDY, KEMP, San Francisco. Died Aug 11, 1991, aged 75. Graduate of University of Oklahoma Medical School, Oklahoma City, 1940. Licensed in California in 1948. Dr Dowdy was a member of the Napa County Medical Society.



FLORIN, ALVIN C., San Bernardino. Died Jul 29, 1991, aged 89. Graduate of University of Illinois, Chicago, 1926. Licensed in California in 1946. Dr Florin was a member of the San Bernardino County Medical Society.



GILMORE, WILLIAM M., Palo Alto. Died Jul 11, 1991, aged 69. Graduate of University of Colorado, Denver, 1949. Dr Gilmore was a member of the Santa Clara County Medical Association.



GOULD, LLOYD E., Yountville. Died Sep 9, 1991, aged 82. Graduate of Loma Linda University School of Medicine, Loma Linda, California, 1934. Licensed in California in 1934. Dr Gould was a member of the Napa County Medical Society.



GULL, REUBEN, Chino. Died Apr 21, 1991, aged 67. Graduate of University of Minnesota Medical School, Minneapolis, 1947. Licensed in California in 1949. Dr Gull was a member of the San Bernardino County Medical Society.

HARTZMAN, ROBERT, Santa Barbara. Died Jun 20, 1991, aged 62. Graduate of State University of New York, 1954. Licensed in California in 1955. Dr Hartzman was a member of the Santa Barbara County Medical Society.



HAWK, WALTER D., Berkeley. Died Jul 21, 1991, aged 85. Graduate of University of Chicago, 1940. Dr Hawk was a member of the Alameda-Contra Costa Medical Association.



HAYES, DONALD MURRAY, San Francisco. Died Aug 17, 1991, aged 66. Graduate of New York College of Medicine, 1951. Licensed in California in 1953. Dr Hayes was a member of the Napa County Medical Society.



JOHNSON, DAVID A., Orange. Died Jul 27, 1991, aged 59. Graduate of Northwestern University, Chicago, Illinois, 1957. Dr Johnson was a member of the Orange County Medical Association.



KOCH, FREMONT P., Camarillo. Died Sep 27, 1991, aged 72. Graduate of Washington University, St Louis, Missouri. Dr Koch was a member of the Ventura County Medical Society.



MCCARTY, KEVIN, San Francisco. Died Aug 8, 1991, aged 69. Graduate of Georgetown University, Washington, DC, 1950. Licensed in California in 1952. Dr McCarty was a member of the San Francisco Medical Society.



MCPHERSON, ALAN GIVEN, Ontario. Died May 10, 1991, aged 64. Graduate of University of Manitoba, Canada, 1951. Licensed in California in 1956. Dr McPherson was a member of the San Bernardino County Medical Society.



MASSENGILL, JAMES B., Ukiah. Died Jul 1, 1991, aged 76. Graduate of University of Tennessee, Memphis, 1937. Licensed in California in 1946. Dr Massengill was a member of the Mendocino-Lake County Medical Society.

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AXID® (nizatidine capsules)

Brief Summary. Consult the package insert for complete prescribing information.
Indications and Usage: 1. Active duodenal ulcer—for up to 8 weeks of treatment. Most patients heal within 4 weeks.

2. Maintenance therapy—for healed duodenal ulcer patients at a reduced dosage of 150 mg h.s. The consequences of therapy with Axid for longer than 1 year are not known.

Contraindications: Known hypersensitivity to the drug. Because cross sensitivity in this class of compounds has been observed, H₂-receptor antagonists, including Axid, should not be administered to patients with a history of hypersensitivity to other H₂-receptor antagonists.

Precautions: General—1. Symptomatic response to nizatidine therapy does not preclude the presence of gastric malignancy.

2. Dosage should be reduced in patients with moderate to severe renal insufficiency.

3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

Laboratory Tests—False-positive tests for urobilinogen with Multistix® may occur during therapy.

Drug Interactions—No interactions have been observed with theophylline, chlorazepoxide, lorazepam, idocaine, phenytoin, and warfarin. Axid does not inhibit the cytochrome P-450 enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of aspirin daily, increased serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently.

Carcinogenesis, Mutagenesis, Impairment of Fertility—A 2-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a 2-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a 2-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect; but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in 1 fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in 1 fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions—Clinical trials of varying durations included almost 5,000 patients.

Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events were due to the drug.

Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to 3 times the upper limit of normal, however, did not significantly differ from that in placebo patients. All abnormalities were reversible after discontinuation of Axid. Since market introduction, hepatitis and jaundice have been reported. Rare cases of cholestatic or mixed hepatocellular and cholestatic injury with jaundice have been reported with reversal of the abnormalities after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in 2 individuals administered Axid and in 3 untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported.

Endocrine—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H₂-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumental—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity—As with other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage: Overdoses of Axid have been reported rarely. If overdose occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis does not substantially increase clearance of nizatidine due to its large volume of distribution.

References

1. Data on file, Lilly Research Laboratories.
2. *Scand J Gastroenterol*. 1987;22(suppl 136):61-70.
3. *Scand J Gastroenterol*. 1987;22(suppl 136):47-55.
4. *Am J Gastroenterol*. 1989;84:769-774.

NZ-2943-B-149347

Additional information available to the profession on request.

Eli Lilly and Company
 Indianapolis, Indiana
 46285



In Memoriam

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MEADOR, JAMES H., San Diego. Died Sep 1, 1991, aged 76. Graduate of University of Arizona, Tucson, 1939. Dr Meador was a member of the San Diego County Medical Society.

MENDA, KISHEN B., Arcata. Died Jul 11, 1991, aged 48. Graduate of G. S. Medical College, India. Dr Menda was a member of the Humboldt-Del Norte Medical Society.

MERRILL, ROBERT L., Hemet. Died Aug 31, 1991, aged 78. Graduate of Washington University, St Louis, Missouri, 1940. Licensed in California in 1946. Dr Merrill was a member of the Riverside County Medical Association.

NESSEROD, JERROLD PEERMAN, Santa Barbara. Died Sep 6, 1991, aged 87. Graduate of Northwestern University, Chicago, Illinois, 1930. Licensed in California in 1947. Dr Nesselrod was a member of the Santa Barbara County Medical Society.

PECK, SAMUEL G., San Diego. Died Sep 1, 1991, aged 82. Graduate of St Louis University, Missouri, 1936. Dr Peck was a member of the San Diego County Medical Society.

PHILLIPS, R. E., Visalia. Died Jul 19, 1991, aged 59. Graduate of University of Rochester, New York, 1958. Licensed in California in 1960. Dr Phillips was a member of the Tulare County Medical Society.

POTTER, GEORGE V., Walnut Creek. Died Jul 13, 1991, aged 78. Graduate of University of Illinois, Chicago, 1938. Dr Potter was a member of the Alameda-Contra Costa Medical Association.

RAY, LEIGHTON W., Santa Rosa. Died Jul 28, 1991, aged 93. Graduate of Harvard Medical School, Boston, Massachusetts, 1924. Dr Ray was a member of the Sonoma County Medical Association.

RICHMOND, ROBERT A., Bakersfield. Died Aug 18, 1991, aged 70. Graduate of New York Medical College, 1949. Licensed in California in 1955. Dr Richmond was a member of the Kern County Medical Society.

SPAUR, R. CRAIG, Riverside. Died Jun 8, 1991, aged 42. Graduate of University of Nebraska College of Medicine, 1980. Licensed in California in 1986. Dr Spaur was a member of the Riverside County Medical Association.

Denver Medical Society

BLANEY, LOREN F. Died Aug 14, 1991, aged 78. Graduate of Washington University, St Louis, Missouri, 1938. Licensed in Colorado in 1951.

LUBCHENCO, MICHAEL A. Died Aug 11, 1991, aged 71. Graduate of University of Colorado Health Sciences Center, Denver, 1945. Licensed in Colorado in 1946.

SCHONEBAUM, ROBERT M. Died Jul 17, 1991, aged 69. Graduate of Creighton University School of Medicine, Omaha, Nebraska, 1945. Licensed in Colorado in 1945.

Idaho Medical Association

GOATES, GREGORY L., Blackfoot. Died Jul 26, 1991, aged 45. Graduate of University of Utah Medical School, Salt Lake City, 1972. Licensed in Idaho in 1985. Dr Goates was a member of the Bingham County Medical Society.

WEHLER, ANDREW J., Riggins. Died Aug 26, 1991, aged 72. Graduate of Jefferson Medical School, Philadelphia, Pennsylvania, 1947. Licensed in Idaho in 1987.

New Mexico Medical Society

GUTOWSKI, FRANZ, Tucumcari. Died Aug 4, 1991, aged 50. Graduate of Dnepropetrovsk Medical Institute, 1938. Licensed in New Mexico in 1969. Dr Gutowski was a member of the Quay County Medical Society.

SPINING, WILLIAM D., Santa Fe. Died Jun 23, 1991, aged 83. Graduate of University of California, 1937. Licensed in New Mexico in 1968. Dr Spining was a member of the Santa Fe County Medical Society.

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